



## cerebrotendinous xanthomatosis

Cerebrotendinous xanthomatosis is a disorder characterized by abnormal storage of fats (lipids) in many areas of the body. People with this disorder cannot break down certain lipids effectively, specifically different forms of cholesterol, so these fats accumulate in the body in the form of fatty yellow nodules called xanthomas. These xanthomas are most commonly found in the brain and in connective tissue called tendons that attach muscle to bone, which is reflected in the condition name (cerebro-meaning brain and -tendinous referring to tendons).

People with cerebrotendinous xanthomatosis often develop neurological problems in early adulthood that are thought to be caused by an abnormal accumulation of fats and an increasing number of xanthomas in the brain. These neurological problems include recurrent seizures (epilepsy), movement disorders, impaired speech (dysarthria), loss of sensation in the arms and legs (peripheral neuropathy), decline in intellectual function (dementia), hallucinations, and depression. Xanthomas can accumulate in the fatty substance that insulates and protects nerves (myelin), causing the destruction of myelin and disrupting nerve signaling in the brain. Degeneration (atrophy) of brain tissue caused by excess lipid deposits also contributes to the neurological problems.

Xanthomas in the tendons begin to form in early adulthood. The most common areas for xanthomas to develop are tendons in the hands, elbows, knees, neck, and in the Achilles tendon, which connects the heel of the foot to the calf muscles in the leg. Tendon xanthomas may cause discomfort and interfere with tendon flexibility. While many affected people develop tendon xanthomas, these nodules may not be easily visible underneath the skin.

Other features of cerebrotendinous xanthomatosis include clouding of the lenses of the eyes (cataracts) and chronic diarrhea in childhood; a reduced ability to produce and release a digestive fluid called bile (cholestasis), which can lead to a yellowing of the skin or whites of the eyes (jaundice); and progressively brittle bones that are prone to fracture (osteoporosis). People with cerebrotendinous xanthomatosis are also at an increased risk of developing cardiovascular disease or respiratory failure because of lipid accumulation in the heart or lungs, respectively. If untreated, the signs and symptoms related to cerebrotendinous xanthomatosis worsen over time; however, this condition varies greatly among those who are affected.

### Frequency

The incidence of cerebrotendinous xanthomatosis is estimated to be 1 per million individuals worldwide. This condition is more common in the Moroccan Jewish population with an incidence of 1 in 108 individuals.

## Genetic Changes

Mutations in the *CYP27A1* gene cause cerebrotendinous xanthomatosis. The *CYP27A1* gene provides instructions for producing an enzyme called sterol 27-hydroxylase. This enzyme works in the pathway that breaks down cholesterol to form acids used in the digestion of fats (bile acids), specifically a bile acid called chenodeoxycholic acid.

Mutations in the *CYP27A1* gene lead to the production of a nonfunction or abnormal sterol 27-hydroxylase that cannot help form chenodeoxycholic acid. As a result, other molecules are formed by an alternative pathway. A molecule called cholestanol, which is similar to cholesterol, is produced as well as substances called bile alcohols. Cholestanol and bile alcohols are increased in the blood, while blood cholesterol levels are typically normal. In various tissues in the body, including the brain and heart, cholesterol and cholestanol levels are increased. These lipids make up much of the fats found in xanthomas. The accumulation of cholesterol and cholestanol throughout the body's tissues causes the signs and symptoms of cerebrotendinous xanthomatosis.

## Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## Other Names for This Condition

- cerebral cholesterinosis
- cerebrotendinous cholesterinosis
- cholestanol storage disease
- cholestanolosis
- CTX
- Van Bogaert-Scherer-Epstein disease

## Diagnosis & Management

### Genetic Testing

- Genetic Testing Registry: Cholestanol storage disease  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0238052/>

### Other Diagnosis and Management Resources

- GeneReview: Cerebrotendinous Xanthomatosis  
<https://www.ncbi.nlm.nih.gov/books/NBK1409>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

### **Additional Information & Resources**

#### MedlinePlus

- Health Topic: Cholesterol  
<https://medlineplus.gov/cholesterol.html>
- Health Topic: Genetic Brain Disorders  
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Lipid Metabolism Disorders  
<https://medlineplus.gov/lipidmetabolismdisorders.html>

#### Genetic and Rare Diseases Information Center

- Cerebrotendinous xanthomatosis  
<https://rarediseases.info.nih.gov/diseases/5622/cerebrotendinous-xanthomatosis>

#### Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Lipid Storage Diseases Information Page  
<https://www.ninds.nih.gov/Disorders/All-Disorders/Lipid-storage-diseases-Information-Page>
- Rare Diseases Clinical Research Network: Sterol & Isoprenoid Research Consortium  
<https://www.rarediseasesnetwork.org/cms/stair/Learn-More/Disorder-Definitions>

### Educational Resources

- CLIMB: Cerebrotendinous Xanthomatosis Info Sheet  
<http://www.climb.org.uk/IMD/Charlie/CerebrotendinousXanthomatosis.pdf>
- Disease InfoSearch: Cerebrotendinous Xanthomatosis  
<http://www.diseaseinfosearch.org/Cerebrotendinous+Xanthomatosis/1249>
- MalaCards: cerebrotendinous xanthomatosis  
[http://www.malacards.org/card/cerebrotendinous\\_xanthomatosis](http://www.malacards.org/card/cerebrotendinous_xanthomatosis)
- Orphanet: Cerebrotendinous xanthomatosis  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=909](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=909)
- Washington Univeristy, St. Louis: Neuromuscular Disease Center  
<http://neuromuscular.wustl.edu/ataxia/metatax.html#cx>

### Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases  
<http://www.climb.org.uk/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/cerebrotendinous-xanthomatosis/>
- United Leukodystrophy Foundation  
<http://ulf.org/cerebrtendinous-xanthomatosis-ctx>

### GeneReviews

- Cerebrotendinous Xanthomatosis  
<https://www.ncbi.nlm.nih.gov/books/NBK1409>

### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22cerebrotendinous+xanthomatosis%22>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28cerebrotendinous+xanthomatosis%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

### OMIM

- CEREBROTENDINOUS XANTHOMATOSIS  
<http://omim.org/entry/213700>

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*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4264335/>

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